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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/248,756	02/12/99	GLIMCHER L	HUI-021CN

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HM12/0620

EXAMINER	
LEFFERS JR, G	
ART UNIT	**PAPER NUMBER**
1636	12

DATE MAILED: 06/20/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary

Application No.	Applicant(s)
09/248,756	Glimcher, et al.
Examiner	**Art Unit**
Gerald G. Leffers Jr.	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *one* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 5, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *35-55* is/are pending in the application.

4a) Of the above, claim(s) *50-55* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *35-49* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Feb 12, 1999* is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Receipt is acknowledged of a preliminary amendment to the specification, filed 8/17/00 as Paper No. 6, wherein applicants have submitted a new paper copy of the sequence listing, corresponding computer-readable form of the sequence listing and corresponding attorney's statement.

Election/Restriction

Applicant's election without traverse of Group I (claims 35-49) in Paper No. 11 is acknowledged.

Claims 35-55 are pending in this application, with claims 50-55 being withdrawn from consideration as being drawn towards a nonelected invention.

Drawings

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ormum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 38 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 13 of U.S. Patent No. 5,958,671 (the '671 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Claim 13 of the '671 patent is drawn toward a method of identifying a compound that modulates the activity of a maf family protein by modulating the ability of the maf family protein to bind a specific DNA sequence, wherein the maf family protein is c-Maf and the method comprises determining the ability of the test compound to affect binding of c-Maf to a maf response element (MARE) of an IL-4 gene regulatory element.

Claim 38 is drawn towards a method of identifying a test compound that modulates an immune response comprising providing an indicator composition (e.g. a test cell or acellular composition), wherein a member of a compound library is first selected for its ability to modulate the activity of the maf family protein member and then subsequently used in an assay to determine its effect on an immune response. Claim 38 specifies that the assay for detection of an effect by a

test compound on an immune response involves monitoring the expression of an interleukin-4 gene.

The patent claim does not specify a further round of screening wherein the identified compound is screened in vivo for its ability to affect IL-4 gene expression. The instant claim does not specify the maf family polypeptide is c-Maf.

It would have been *prima facie* obvious for one of ordinary skill in the art to further test a compound identified by the method of the patent claim to modulate the binding of c-Maf to an IL-4 gene regulatory element to further include an additional round of testing with a cellular indicator composition because c-Maf is particularly claimed in the patent as a maf family polypeptide which will specifically bind to an IL-4 gene regulatory element. One would have been motivated to do so in order to receive the expected benefit of possibly obtaining a compound which could modulate IL-4 expression in a cellular environment. Absent any evidence to the contrary, there would have been a reasonable expectation of success in practicing the invention of the patent claim wherein an identified compound which modulates binding of c-Maf to an IL-4 regulatory element is further tested with an indicator composition comprising an intact cell. Therefore, claim 38 is merely an obvious variant of claim 13 from the '671 patent.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn towards methods for identifying a compound that modulates an immune response, comprising providing an indicator composition comprising a "maf family protein" and target DNA to which this class of transcriptional regulators binds specifically. The indicator composition is contacted with each member of a library of test compounds and members are selected which modulate the transcriptional regulatory activity of the maf family protein. The selected modulatory compounds are then used to determine "the effect of the compound of interest on an immune response to thereby identify a compound that modulates an immune response.". The maf family protein can be any "maf family" transcriptional regulator, or specifically c-Maf, v-maf, mafB, Nr1, mafK, mafF, mafG or p18. The host indicator cell can be any cell, or can specifically be a T helper type 1 (Th1) or T helper type 2 (Th2) cell. The target DNA can be any target DNA bound by a maf family protein, or specifically a regulatory sequence of a Th2-associate cytokine gene (e.g. IL-4). The indicator composition can be a cell (e.g. a lymphoid cell, Th2 cell, Th1 cell) or an acellular composition.

The claims are enormously broad genus claims with regard to the potential polypeptides to be assayed (i.e. potential maf family member polypeptides) and with regard to the type of immune response to be assayed following determination that a compound modulates the activity of a maf family member polypeptide. Such assays would encompass, for example, stimulation of a general or specific antibody response, stimulation of specific or general T-cell response, repression of specific T-cell or B-cell response, stimulation of complement cascade response, recognition of "self" antigens, etc. The screening assays contemplated at the time of filing are described on pages 36-40 of the specification. The only maf family protein described in the specification or prior art to be associated with a cell involved in immune response is c-Maf. The instant specification describes c-Maf as being a positive regulator of IL-4 transcription in Th2 cells. There is no description of any maf family protein being involved in expression of any other cytokine genes from any cell type.

Given the lack of description from the specification for immune response assays, the lack of an adequate description of what constitutes a "maf family" protein, and the lack of description of any maf family polypeptide in the specification or prior art which is involved in any clear way with an immune response, except for c-Maf and IL-4 expression, one of skill in the art would not be able to envision a representative number of the methods of the claimed invention. Therefore, one of skill in the art would reasonably conclude that applicants were not in possession of the claimed invention.

Claims 35-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments wherein the immune response monitored is the immune response assayed is the effect of the test compound on expression of a an interleukin-4 gene and wherein the maf family protein is c-Maf, does not reasonably provide enablement for practicing the claimed invention with any other immune response and with any other maf family proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. .

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the art, state of the prior art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

The rejected claims are broadly drawn towards screening methods involving a final step of determining the effect of a compound, identified as modulating maf-dependent transcription, on an immune response. This step broadly encompasses all methods of determining the effects on all immune responses. The specification as originally filed provides no guidance on a method having this final step. The prior art does not remedy the deficiency. From the background provided in the specification, one of skill in the art might expect the compounds of interest to affect the maturation of Th2 cells in vivo based upon modulation of the activity of c-Maf, a positive regulator of IL-4 expression. However, there is no guidance as to the types of assays that could

be employed to determine the effect of the compounds of interest on an immune response involving these expected, induced phenotypes. No guidance is presented as to possible effects on any other types of immune response, or any assays for determining such. The screening assays contemplated at the time of filing are described on pages 36-40 of the specification. The only maf family protein described in the specification or prior art to be associated with a cell involved in immune response is c-Maf. The instant specification describes c-Maf as being a positive regulator of IL-4 transcription in Th2 cells. There is no description of any maf family protein being involved in expression of any other cytokine genes from any cell type. In the almost complete lack of guidance in the specification, the rejected claims amount to an invitation to trial and error experimentation as well as novel inventive and research efforts to develop the necessary assays to determine whether there are any other types of immune responses that might be affected and if such responses can be detected at a statistically meaningful level.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is vague and indefinite in that the claim is grammatically incorrect. The phrase "said maf family protein bind," should be amended to read "said maf family protein binds".

Claims 35, 37-39, 41-49 are vague and indefinite in that the metes and bounds of the phrase "a Maf family protein" are unclear. The specification has not defined "Maf family protein" in such a way as to allow one skilled in the art to distinguish between a member of "Maf family" of bZIP transcription factors (e.g. c-Maf) and a member of the broader super family of bZIP transcription factors (e.g. AP-1) that would not be a Maf protein (e.g. c-Jun). While some transcription factors have been identified in the art as being "Maf" proteins (e.g. MafB, MafK, Nr1, etc.), it is unclear from the specification how one skilled in the art would determine whether a newly discovered AP-1 transcription factor were a Maf protein or not. The distinguishing characteristics of a Maf protein have not been provided in the specification and its is unclear that there are art recognized standards for identifying a Maf protein distinct from any other bZIP factor. The prior art only shows those proteins that are well within the metes and bounds of "Maf family protein" and provides no guidance for determining whether any other members of the bZIP family of transcription factors, known and unknown, are meant to be included in the instant invention.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official

Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Leffers, Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Dr. Rob Schwartzman, can be reached on (703) 308-7307.

Any inquiry of a general nature or relating to the status of this application, or relating to attachments to this office action, should be directed to the Patent Analyst Zeta Adams, whose telephone number is (703) 305-3291.

GLL

G. Leffers, Jr.

Patent Examiner

Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER

June 18, 2001